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PATENT TRADEMARK OFFICE

Docket No: 2094/EP86US1
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Kevin M. GORMAN, David R. PATTERSON,
Jeffrey M. LINNEN and Keming SONG

Serial No.: 09/494,332

Art Unit: 1655

Filed: January 28, 2000

Examiner: J. GOLDBERG

For: OLIGONUCLEOTIDE PRIMERS FOR EFFICIENT MULTIPLEX DETECTION OF
HEPATITIS C VIRUS (HCV) AND HUMAN IMMUNODEFICIENCY VIRUS (HIV)
AND METHODS OF USE THEREOF

RESPONSE TO OFFICE ACTION
UNDER 37 C.F.R. §1.116

Hon. Commissioner of Patents and Trademarks
BOX AFTER FINAL
Washington, DC 20231

Sir:

In response to the Office Action mailed on September 19, 2001 for
this application and in accordance with Rule 116 of the Rules of Practice, please
enter and consider the following remarks. Applicants submit concurrently herewith:

(1) a Declaration of Kevin M. Gorman Under 37 C.F.R. § 1.132 (the "Gorman Declaration"), including Exhibits 1-2; (2) a Petition for Extension of Time, requesting that the time period for responding to the Office Action be extended for a period of two month (*i.e.*, from December 19, 2001 up to and including February 19, 2002) and accompanied by the appropriate fee; and (3) a Notice of Appeal, accompanied by the appropriate fee.

It is believed that no additional fees are required for these submissions. However, should the U.S. Patent and Trademark Office determine that the payment of any additional fee is required or that any refund is owed for this application, the Commissioner is hereby authorized and requested to charge the required fee(s) and/or credit the refund(s) due to our Deposit Account No. 04-0100.

REMARKS

Claims 1-46 are pending in this application. Applicants note, with appreciation, that the Examiner has found claims 25 and 46 to be allowable. The Examiner has objected to claims 32, 34, 36, 38, 40 and 42 as depending from a rejected base claim, but indicates that these claims would be allowable if rewritten in independent form. However, the Examiner has maintained the previous rejection of claims 1-24, 26-31, 33, 35, 37, 39, 41 and 43-45 under 35 U.S.C. § 103(a), and has also maintained the provisional rejection of claims 1-15 for obviousness-

type double patenting. Applicants respond to each of these rejections in detail below.

THE REJECTIONS UNDER 35 U.S.C. § 103(a)
SHOULD BE WITHDRAWN

The Examiner has maintained the rejection of claims 1-24, 26-31, 33, 35, 37, 39, 41 and 43-45 as being obvious over various combinations of the following references:

- (1) Han *et al.*, "Characterization of Conserved Sequences in the 5' Untranslated Region and Poly(A) Tails and the 3' End", *Proc. Natl. Acad. Sci. U.S.A.* 1991, 88:1711-1715 ("Han");
- (2) U.S. Patent No. 5,846,704 issued December 8, 1998 to Maertens *et al.* ("Maertens");
- (3) U.S. Patent No. 6,001,558 issued December 14, 1999 to Backus *et al.* ("Backus");
- (4) Nedjar *et al.*, "Co-Amplification of Specific Sequences of HCV and HIV-1 Genomes by Using the Polymerase Chain Reaction Assay: A Potential Tool for the Simultaneous Detection of HCV and HIV-1", *J. of Virological Methods* 1991, 35:297-304 ("Nedjar"); and

- (5) Ahern, "Biochemical Reagent Kits Offer Scientists Good Return on Investment", *The Scientist* 1995, 9(15):20 ("Ahern")¹

Briefly, the Examiner has indicated that Han and Maertens both teach a conserved region of the HCV genome, referred to as the 5'-untranslated region (5'-UTR), and its use for genotyping HCV. The Backus reference allegedly relates to oligonucleotides for the amplification and detection of human immunodeficiency virus (HIV) RNA, and Nedjar is cited as teaching a particular multiplex PCR assay that simultaneously amplifies and detects nucleic acids from both HCV and HIV. Finally, the Ahern reference discusses the utility and desirability of kits for biological assays in general, but is not related *per se* to the amplification or detection of any nucleic acid.

The Examiner has acknowledged that none of the cited references specifically teaches the amplification or detection of either HCV or HIV using the particular primer set recited in the pending claims. However, the Examiner argues that the particular HCV-specific primer sequences of this invention would have been obvious to persons skilled in the art, given the full length HCV 5'-UTR sequence taught by Hans and Maertens and the HIV-specific sequences taught by Backus. The Examiner then concludes that the Nedjar reference would motivate those skilled

¹ This reference has been cited in the Office Action by the internet web page: www.thescientist.library.upenn.edu/yr1995/july/tools_950724.html, December 22, 1998.

in the art to combine the particular primers in a multiplex PCR assay, and that a person skilled in the art would have had a reasonable expectation of success when making such a combination.

In response, Applicants respectfully submit that these obviousness rejections have been made in error and should be withdrawn. Even if a skilled artisan might have been motivated to use the specific primer sequences of this invention *individually* for detecting HCV and HIV (*i.e.*, in separate assays), the combined use of such primers in an assay of the present invention (*i.e.*, for the *simultaneous* detection of both HCV and HIV in a single assay) would not have been obvious to a skilled artisan when this invention was first filed. Specifically, and contrary to what is stated in the Office Action, a skilled artisan could not have had a reasonable expectation of success in using these primers for such a multiplex PCR assay.

To better demonstrate this point, Applicants respectfully direct the Examiner's attention to the Declaration of Kevin M. Gorman Under 37 C.F.R. § 1.132 (the "Gorman Declaration"), which is submitted concurrently herewith.² The Gorman Declaration describes experiments in which the named inventors of this application tested various combinations of HCV- and HIV-specific primers to

² Applicants wish to point out that the Gorman Declaration mistakenly identifies the Declarant's former employer, Ortho-Clinical Diagnostics, Inc., as a "subsidiary" of Johnson & Johnson, Co. See, specifically, ¶ 2 of the Gorman Declaration. The Declaration should properly state that Ortho-Clinical Diagnostics is an "affiliate" of Johnson & Johnson, Co. Applicants and Declarant regret this inadvertent error.

determine which combination(s), if any, could be used in a clinical assay. In one experiment, the inventors tested the particular primer set(s) recited in the pending claims of this patent application, including HCV-specific primers derived from the 5'-UTR region described by Han and Maertens (see, ¶ 10 of the Gorman Declaration).³ However, the inventors also tried a multiplex PCR assay with a different combination of primers. In particular, this other assay used HCV-specific primers from a region of the HCV genome that the Gorman Declaration describes as the 3' non-coding ("NC") region.

Like the 5'-UTR, the 3' NC region is a portion of the HCV genome that is known to be highly conserved and useful for detecting HCV nucleic acids, *e.g.*, in PCR assays. See, ¶ 8 of the Gorman Declaration. See, also, Kolykhalov *et al.*, "Identification of a Highly Conserved Sequence Element at the 3' Terminus of Hepatitis C Virus Genome RNA" *J. Virol.* 1996, 70:3363-3371 ("Kolykhalov").⁴ Yet, HCV-specific primers derived from this region completely fail to work in a multiplex PCR assay. In particular, the Gorman Declaration demonstrates that, when HCV-specific primers derived from the 3' NC region are used in combination with the HIV-specific primers of this invention, an intense side product band is observed so that "a viable assay could not be made using that combination of

³ Applicants note that both the Gorman Declaration and the instant application refer to the 5'-UTR taught by Han as the 5' non-coding ("NC") region of the HCV genome.

⁴ The Kolykhalov reference is discussed in ¶ 8 of the Gorman Declaration, and is attached to that Declaration at Exhibit Tab 2.

primers." See, in particular, ¶ 14 of the Gorman Declaration. Only by using the particular combination of HIV- and HCV-specific primers recited in the pending claims was it possible to construct a viable clinical assay for simultaneously detecting both viruses in a sample. See, ¶ 13 of the Gorman Declaration. See, also, the Example at pages 17-20 of this application as filed.

At the very best, therefore, the combination of references cited by the Examiner could have only motivated a skilled artisan to *try* using the particular primers recited in the pending claims in an assay method of this invention, However, "obvious to try" is not the standard for obviousness under 35 U.S.C. § 103(a). For a claimed invention to be obvious under the patent statute, the skilled artisan must also have a reasonable expectation of success. The Gorman Declaration demonstrates, however, that a skilled artisan could not have reasonably expected such an assay to succeed.

For all of these reasons, Applicants submit that the rejection under 35 U.S.C. § 103(a) has been made in error, and respectfully request that the rejection be withdrawn.

THE NONSTATUTORY DOUBLE PATENTING REJECTION

Applicants note that the Examiner has maintained the provisional rejection of claims 1-15 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-64 in copending patent

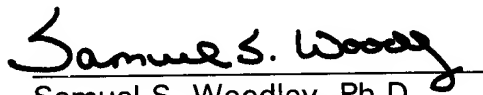
application serial no. 09/493,353 ("the '353 application"). Because this is a provisional rejection, Applicants respectfully decline to respond to the rejection at this time. However, Applicants agree to submit a terminal disclaimer should the Examiner maintain this rejection upon a finding of allowable subject matter in the two applications.

CONCLUSION

For the reasons stated above, Applicants believe that the Examiner's rejections of the pending claims have been overcome and that the claims, as amended, are in condition for allowance. Accordingly, the withdrawal of all objections and rejections, and reconsideration of the application are respectfully requested. The Examiner is invited to contact Applicants' undersigned representative at the below indicated telephone number if she believes it may advance prosecution of this application. An allowance is earnestly sought.

Respectfully submitted,

Dated: February 19, 2002


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